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Endocrine cells in the anal canal

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Summary. Endocrine cells are normal inhabitants of the anal canal. While numerous endocrine cells are distributed throughout anal ducts and crypts, few are dispersed in the anal transitional zone. All these cells were characterized as serotonin-storing cells, and this endocrine profile is quite distinctive from that of adjacent mucosae. Rectal epithelium contains serotonin, somatostatin, enteroglucagon, BPP and HPP immunoreactive cells; endocrine cells are lacking in the pectinal folds and perianal skin. It is suggested that this distinctive hormonal profile may be regarded as a specific marker of this anal territory. The same pattern is found in the fetal transitional lining of anal canal.

Evidence of serotonin-storing cells in the transitional epithelium of anal glands and crypts and in the ATZ epithelium, reinforces the homology between these linings and urothelium. The presence of a similar fetal epithelium implies that ATZ epithelium in adults is not necessarily metaplastic. All derivatives of the cloaca may therefore share the same endocrine profile.

Key words: Anal canal – Endocrine cells – Serotonin-storing cells – Anal ducts – Fetus

Introduction

Since the first studies of Feyrter (1934), endocrine cells in the gastrointestinal tract have been extensively analysed. In contrast, those of the anal canal have received comparatively little attention. The histological features of the anal canal were documented by Hermann and Desfosses in 1880, and subsequently by several other authors. Among them, only Fenger and Knoth (1981) and Hervé de Sigalony et al. (1983) mentioned endocrine cells in the anal transitional zone epithelium.

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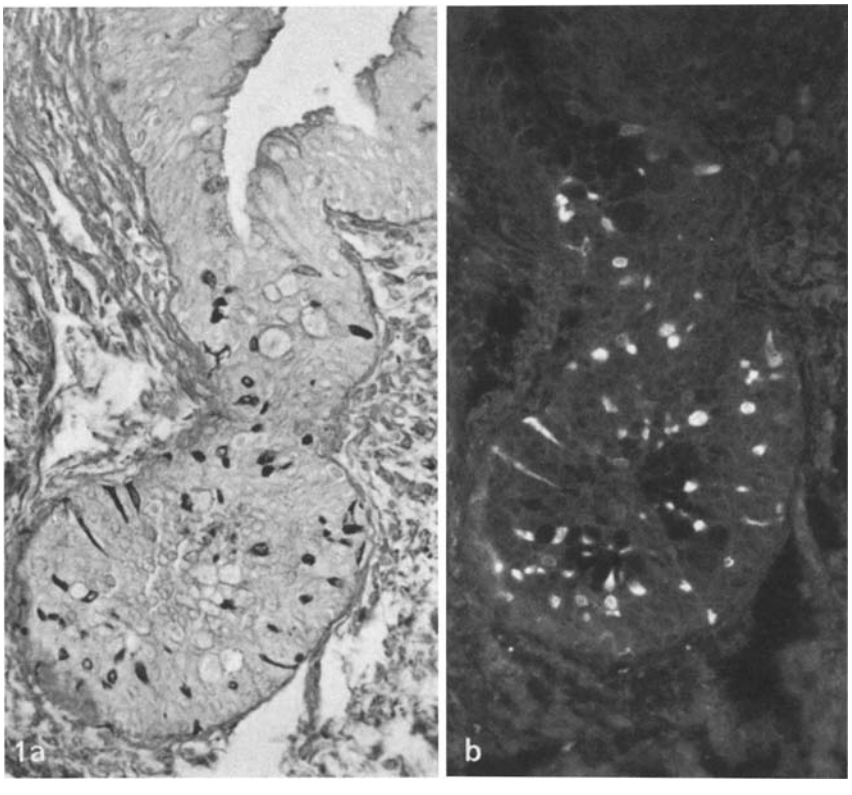


Fig. 1 a, b. Anal duct opening into a crypt. (**a**) Numerous argyrophilic cells are distributed through the anal duct. Grimelius ×170. (**b**) Same section after serotonin immunofluorescence ×200. Note the closely similar distribution of argyrophilic (**a**) and serotonin-storing cells (**b**)

In the urogenital tract, serotonin-storing cells are invariably found throughout transitional epithelium derived from the cloaca (Fetissof et al., 1983). In view of these results, we were led to search for endocrine cells in the anal canal. Adult and fetal specimens were investigated using the argyrophilic Grimelius procedure as well as immunohistochemical and ultrastructural technics.

Materials and methods

The material comprised 6 abdomino-perineal resections for adenocarcinomas of the sigmoid colon and rectum. Were also included examples of basaloid (cloacogenic) carcinomas (5) and surgical haemorrhoidectomy specimens (5). This material provided an opportunity to study colo-rectal type mucosa, anal transitional zone, anal ducts, pecten and perianal skin with circumanal sweat-glands. In addition, one 16-week-old fetus was investigated.

All tissue samples were fixed in aqueous Bouin's fluid and then embedded in paraffin. A modified Grimelius reaction was used to detect argyrophilic cells. All specimens containing argyrophilic cells were investigated immunohistochemically.

Indirect immunofluorescence was performed on deparaffinized sections with rabbit antisera to ACTH, gastrin, glucagon, motilin, neurotensin, serotonin, somatostatin, with guinea pig

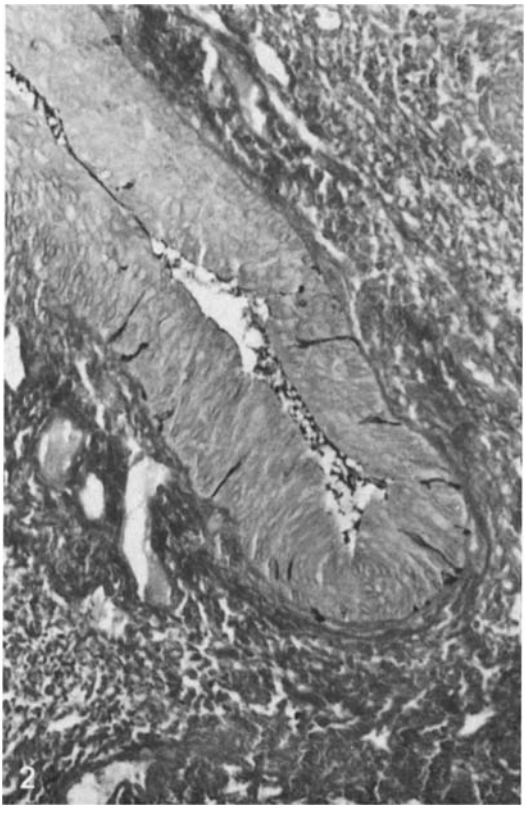


Fig. 2. Anal crypt. Endocrine cells are essentially confined to the bottom of the crypt, which is lined by a transitional epithelium. Grimelius ×140

antiserum to insulin, and with sheep antiserum to calcitonin. Anti-glucagon immune serum was kindly furnished by Dr R. Assan (Hôpital Bichat, Paris) and all other immune sera by Dr M.P. Dubois (INRA, Station de Physiologie de la Reproduction, Nouzilly). Working dilutions varied from 1/50 to 1/100. In order to investigate the relative distribution of argyrophilic or argentaffin cells to immunoreactive cells, combined technics were applied sequentially to the same sections. Grimelius or Masson-Fontana stain was carried out first. Silver deposits were removed by treatment of the sections with potassium cyanide (1%); lastly, immunofluorescence was performed. – Fragments of anal mucosa were fixed in glutaraldehyde for ultrastructural study.

Results

The anal canal lining presented a wide range of histological appearances. These variations characterized the anal transitional zone (ATZ). This zone was interposed between uninterrupted crypt-bearing colo-rectal type mucosa above and stratified squamous epithelium below. The ATZ exhibited a distinctive stratified columnar epithelium, referred to in the following text as ATZ epithelium. ATZ was not always identified; when present, this segment was of variable extent. ATZ was lined either by ATZ epithelium alone or, by areas of ATZ and squamous epithelia in succession. Sometimes, at the junction with rectal type mucosa, an interpenetration of epithelia

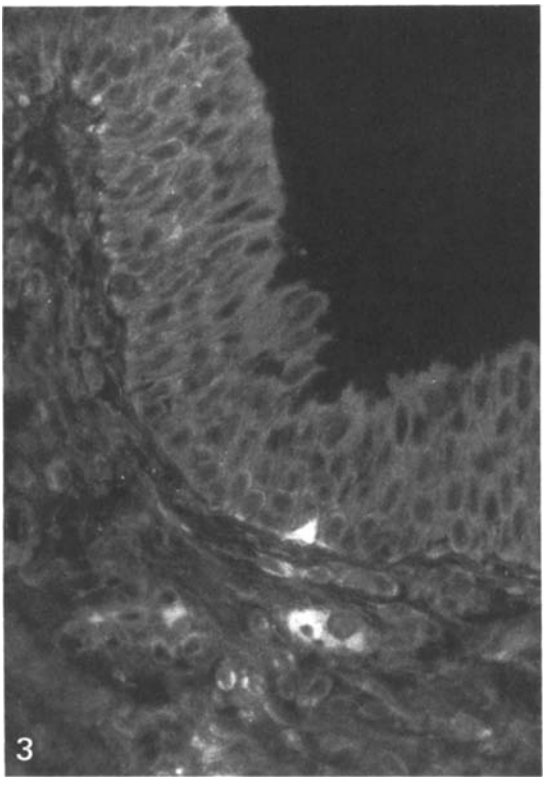


Fig. 3. An isolated serotonin-storing cell in ATZ epithelium. ×280

reproduced a pattern somewhat similar to that of the cervical transformation zone; colo-rectal crypts were overlaid by islands of stratified squamous or columnar epithelium. Anal ducts and bottom of anal crypts had an epithelial lining of the transitional type. This remarkable epithelium displayed a tendency to differentiate into mucinous cells at the surface.

Endocrine cells were detected in the anal canal, throughout the anal ducts, crypts and transitional zone. These distinctive cells were clearly disclosed by the argyrophilic Grimelius procedure. All immunofluorescence studies were negative except for the antiserotonin preparations which revealed positive cells. Combined techniques, using Grimelius and serotonin immunofluorescence, demonstrated a close similarity between the distribution of endocrine argyrophilic cells and serotonin-storing cells (Fig. 1).

Anal ducts (Fig. 1) and the bottom of anal crypts (Fig. 2) proved particularly rich in endocrine cells. Some anal ducts seemed almost entirely covered with serotonin-storing cells. The ATZ contained a small number of serotonin-storing cells. They were essentially confined to areas of ATZ epithelium (Fig. 3); however, some rare positive cells could be encountered in squamous epithelium.

Electron microscopic study permitted the identification of cells which contained dense granules averaging 120 nm in diameter (Fig. 4).

Fig. 4. Endocrine cell contains numerous dense cytoplasmic granules. ×18,000

Occasional melanocytes were observed in the squamous lining of ATZ, sometimes in the close vicinity of colo-rectal crypts. These cells were characterized by combined techniques using Masson-Fontana and serotonin immunofluorescence. They were argentaffin, whereas serotonin immunoreactivity was negative.

No endocrine cells were detected in the squamous lining of the pectinal folds or in perianal skin. In this territory, numerous melanocytes were present. Circumanal sweat-glands were devoid of argyrophilic cells.

Rectal type mucosa was richly endowed with endocrine cells immunoreactive for serotonin, glucagon and somatostatin.

No endocrine cells were demonstrated in basaloid cloacogenic carcinomas; some of these neoplasms harbored a variable number of melanocytes.

In the fetus, between the intestinal columnar epithelium and the stratified squamous epithelium of proctodaeum was intercalated a long segment, lined by a transitional epithelium. Transitions between the 3 varieties of linings were well defined (Fig.5).

Numerous endocrine cells were dispersed in intestinal and transitional epithelium; in contrast no endocrine cells were identified in the squamous

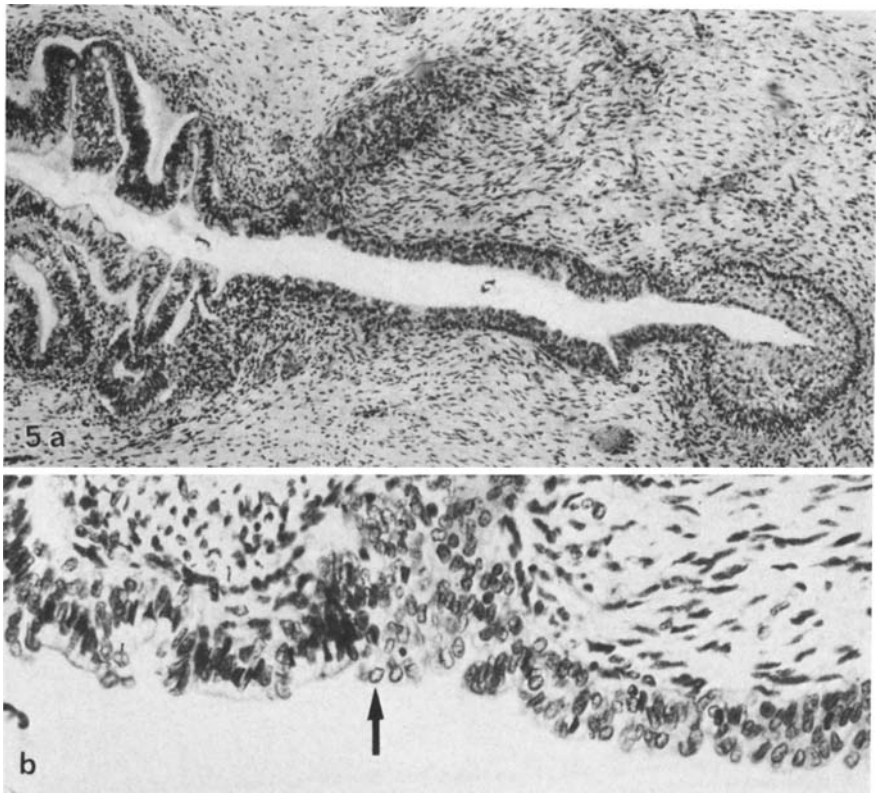
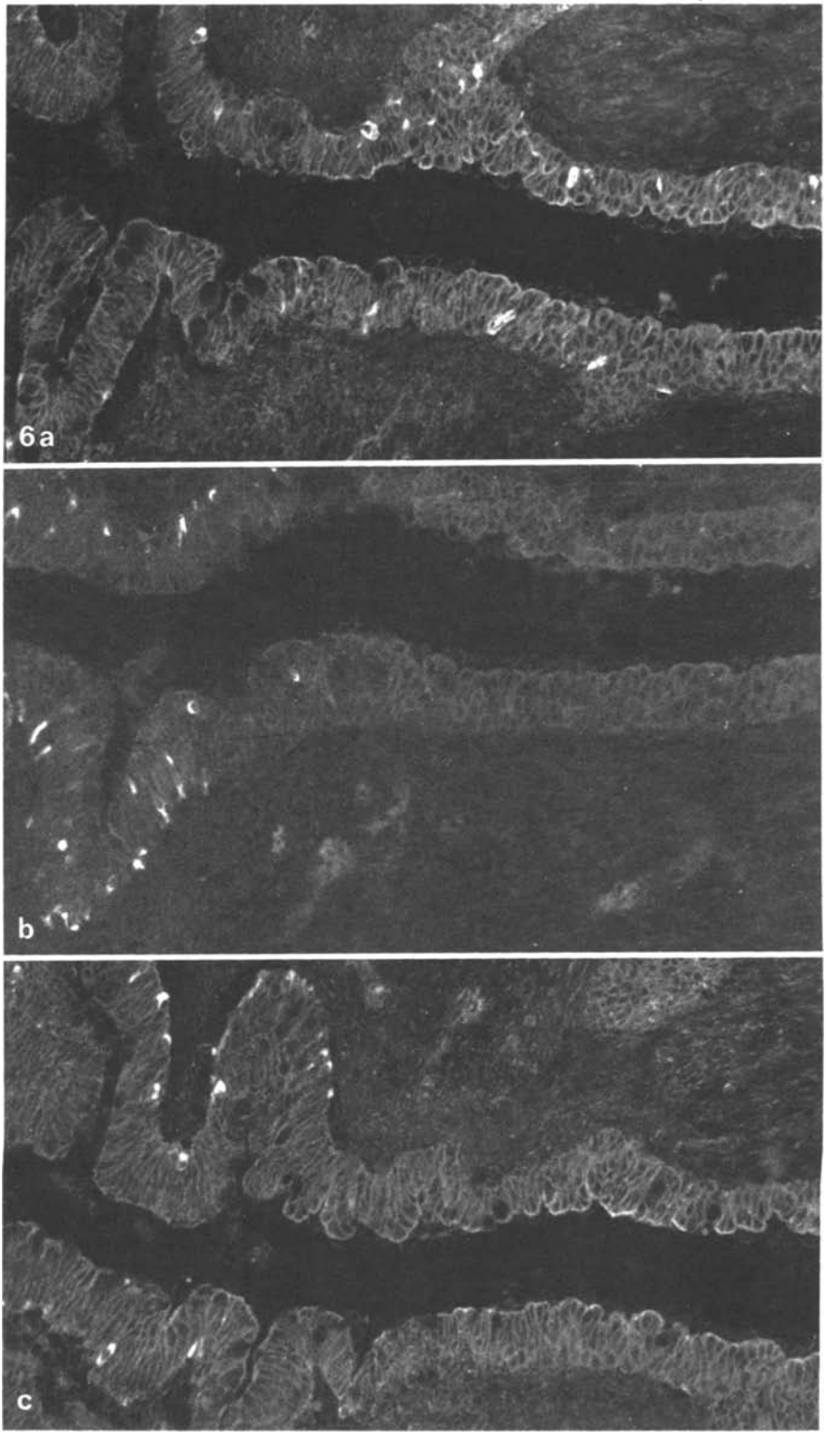


Fig. 5a, b. Fetus. (**a**) General histological appearance of anal area. A segment lined by transitional epithelium is interposed between intestinal mucosa at left, and squamous proctodaeum at right. HES ×40. (**b**) Higher magnification of the abrupt junction (arrow) between the intestinal and transitional linings. HES ×180

epithelium of proctodaeum. The intestinal mucosa contained serotonin, glucagon and somatostatin immunoreactive cells. In contrast, serotonin-storing cells were the only positive cells detected among the transitional epithelium (Fig. 6). In this site, combined technics using Grimelius and serotonin immunofluorescence demonstrated a close similarity between the distribution of argyrophilic and serotonin-storing cells. The junction between intestinal and transitional epithelia was underlined by the dramatic dissappearance of glucagon and somatostatin immunoreactive cells. Similarly, serotonin-storing cells abruptly disappeared at the meeting with the proctodaeum.

In the same preparations, serotonin-storing cells were identifiable in urethral transitional epithelium and prostate gland.

Fig. 6a–c. Fetus. Intestinal mucosa at left, transitional mucosa at right. Serotonin-storing cells (**a**) are distributed through the intestinal and transitional epithelium. Glucagon (**b**) and somatostatin (**c**) immunoreactive cells are confined to the intestinal mucosa. ×130


6a
b
c

Discussion

Several authors have documented the morphological features of the anal canal (Hermann and Desfosses 1880; Grinvalsky and Helwig 1956; Fenger 1979). The considerable range of variation in the histology of this region has been previously detailed by Walls (1958). Ultrastructural studies of the ATZ epithelium were undertaken by Gillespie and MacKay (1978), Fenger and Knoth (1981), Devaux et al. (1982) and Hervé de Sigalony et al. (1983).

Two types of endocrine cells were identified by Fenger and Knoth (1981) on the basis of an ultrastructural investigation of ATZ epithelium. The cells contained granules 4–500 nm and 100 nm in diameter. We only characterized one population of endocrine cells, the serotonin-storing cells. Granule diameters averaged 120 nm. These specialized cells were distributed through anal ducts, crypts and transitonal zone. In the fetus, serotonin-storing cells were again the only endocrine cells found in the transitional epithelium of anal canal. Such an endocrine pattern was quite distinctive from that of adjacent mucosae. This finding reinforces the individuality of the anal canal. Rectal mucosa contained a great variety of endocrine cells, immunoreactive for serotonin, enteroglucagon and somatostatin; most of the enteroglucagon-containing cells presented BPP and possibly HPP immunoreactivities (Lehy and Cristina 1979; Fiocca et al. 1980; O'Briain et al. 1982). In contrast, endocrine cells were lacking in the squamous lining of the pectinal folds and perianal skin. Therefore, this distinctive hormonal profile may prove to be of value as a specific marker of this anal territory.

It must be pointed out that we did not undertake a specific search for amphicrine cells or "enterochromaffin nervefibre complexes" as documented in the appendix by Höfler et al. (1982).

ATZ epithelium has given rise to contradictory statements. The resemblance of ATZ epithelium to the urothelium of the excretourinary tract was stressed by Tucker and Hellwig (1935), Grinvalsky and Helwig (1956), Gillespie and MacKay (1978) and Devaux et al. (1982). These authors considered ATZ epithelium to be a persistent remnant of the cloaca. According to Fenger and Knoth (1981), the fine structure of ATZ epithelium and urothelium differed appreciably. On this ground, Fenger and Knoth (1981) suggested that ATZ epithelium might be metaplastic epithelium, as observed in the cervical transformation zone, rather than true urothelium.

Serotonin-storing cells are the only endocrine cells normally found throughout the transitional epithelium of urethra and its adnexal glands (Fetissof et al. 1983). On the other hand, no endocrine cells are usually detected in the metaplastic squamous epithelium of the cervical transformation zone. Therefore, the presence of a unique population of endocrine, serotonin-storing cells in the epithelial lining of anal ducts, crypts and transitional zone reproduces an endocrine profile somewhat similar to that of urethra. This fact reinforces the analogy between urothelium and the transitional epithelium of anal ducts or crypts. In the same way, this finding brings support to the suggestion that stratified columnar ATZ epithelium should be a variant of urothelium.

Evidence of a fetal transitional epithelium exhibiting the same pattern of hormonal expression would invalidate the argument that the occurrence of such an epithelium in the ATZ of an adult, is necessarily an example of metaplasia.

All these considerations should be qualified at the junction with rectal type mucosa. As mentioned previously, a situation morphologically similar to the cervical transformation zone was sometimes realized. Colo-rectal crypts were occasionally overlaid by islands of stratified squamous or columnar epithelium. It may be thought that, in contrast to ATZ epithelium, the small foci of stratified columnar epithelium which overlap rectal crypts, develop from the native intestinal mucosa, through a metaplastic process.

Serotonin-storing cells are normal inhabitants of organs which originated from the urogenital sinus. Observations on the anal canal provide evidence that the same endocrine profile is actually shared by all tissues derived from cloaca.

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